F. ENT COOPERATION TREA. .

	From the INTERNATIONAL BUREAU			
PCT	То:			
NOTIFICATION OF ELECTION (PCT Rule 61.2)	United States Patent and Trademark Office (Box PCT) Crystal Plaza 2 Washington, DC 20231 ÉTATS-UNIS D'AMÉRIQUE			
Date of mailing (day/month/year)	in its capacity as elected Office			
21 April 1999 (21.04.99)				
International application No. PCT/JP98/03980	Applicant's or agent's file reference 1082			
International filing date (day/month/year)	Priority date (day/month/year)			
04 September 1998 (04.09.98)	05 September 1997 (05.09.97)			
Applicant				
SHIMADA, Junichi et al				
1. The designated Office is hereby notified of its election made X in the demand filed with the International Preliminary 31 March 1999	(Examining Authority on: (31.03.99) national Bureau on:			
The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland	Authorized officer Sean Taylor			

Telephone No.: (41-22) 338.83.38

Facsimile No.: (41-22) 740.14.35

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PCT

REQUEST

For receiving Office use only	
international Application No.	
International Filing Date	
Name of receiving Office and "PCT International	Application"

The undersigned requests that the present international application be processed according to the Patent Cooperation Treaty.	Name of receiving Office and "PCT International Application"					
	Applicant's or agent's file reference (if desired) (12 characters maximum) 1082					
Box No. I TITLE OF INVENTION						
THERAPEUTIC AGENT FOR NEURODEC	SENERATIVE DISORDERS					
Box No. II APPLICANT						
Name and address: (Family name followed by given name; for a designation. The address must include postal code and name of co address indicated in this Box is the applicant's State (that is, country of residence is indicated below.)	n legal entity, full official nuntry. The country of the ry) of residence if no State This person is also inventor.					
Kyowa Hakko Kogyo Co., Ltd.	Telephone No.					
Ryowa nakko kogyo co., 200.	03-3282-0036 Facsimile No.					
6-1, Ohtemachi 1-chome, Chiyoda-ku, Tok						
·	Teleprinter No.					
State (that is, country) of nationality: JP	State (that is, country) of residence: JP					
This person is applicant all designated all designated for the purposes of:	ted States except States of America only the States indicated in States of America only the Supplemental Box					
Box No. III FURTHER APPLICANT(S) AND/OR (FUR)	THER) INVENTOR(S)					
Name and address: (Family name followed by given name: for a designation. The address must include postal code and name of coaddress indicated in this Box is the applicant's State (that is, country of residence is indicated below.) SHIMADA Junichi Royal Hills Nibankan #305, 98-1, Nameri Sunto-gun, Shizuoka 411-0933 Japan	This person is: applicant only applicant and inventor					
	is marked, do not fill in below.)					
State (that is, country) of nationality: JP	State (that is, country) of residence: JP					
This person is applicant all designated for the purposes of: all designated all designated the United States	the States except States of America The United States States of America only The States indicated in the Supplemental Box					
X Further applicants and/or (further) inventors are indicated	on a continuation sheet.					
Box No. IV AGENT OR COMMON REPRESENTATIVE	E; OR ADDRESS FOR CORRESPONDENCE					
The person identified below is hereby/has been appointed to act of the applicant(s) before the competent International Authorities						
Name and address: (Family name followed by given name: for a designation. The address must include postal c	a legal entity, full official code and name of country.)					
	Facsimile No.					
•	Teleprinter No.					
•	Acceptance 140.					
Address for correspondence: Mark this check-box where space above is used instead to indicate a special address to	no agent or common representative is/has been appointed and the which correspondence should be sent					

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Chartai	2	
Sheet No.		

Continuation of Box No. III FURTHER APPLICANT(S) AND/OR (FURTHER) INVENTOR(S)								
If none of the following sub-boxes is used, this sheet should not be included in the request.								
Name and address: (Family name followed by given name: for a l designation. The address must include postal code and name of cour address indicated in this Box is the applicant's State (that is, country, of residence is indicated below.) KUROKAWA Masako 656-18, Yasuhisa, Mishima-shi, Shizuoka	This person is: applicant only X applicant and inventor inventor only (If this check-box is marked, do not fill in below.)							
State (that is, country) of nationality:	State (that is, country)	Facidation						
JP	State (mar is, country)	JP						
		United States the States indicated in the Supplemental Box						
Name and address: (Family name followed by given name; for a lidesignation. The address must include postal code and name of cour address indicated in this Box is the applicant's State (that is, country) of residence is indicated below.) IKEDA Ken Kureru Takehara #211, 336-1, Takehara, N. Sunto-gun, Shizuoka 411-0944 Japan	itry. The country of the of residence if no State	This person is: applicant only applicant and inventor inventor only (If this check-box is marked, do not fill in below.)						
State (that is, country) of nationality:	State (that is, country) o	1						
JP This person is applicant all designated all designated all designated	States event	JP						
		United States America only the States indicated in the Supplemental Box						
Name and address: (Family name followed by given name; for a le designation. The address must include postal code and name of coun address indicated in this Box is the applicant's State (that is, country) of residence is indicated below.) SUZUKI Fumio 18-4, Fujimidai, Mishima-shi, Shizuoka 4	of residence if no State	This person is: applicant only X applicant and inventor inventor only (If this check-box is marked, do not fill in below.)						
State (that is, country) of nationality:	State (that is, country) of	of residence:						
JP		JP						
This person is applicant all designated all designated for the purposes of: all designated the United States		United States America only the States indicated in the Supplemental Box						
Name and address: (Family name followed by given name: for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant 'sState (that is, country) of residence if no State of residence is indicated below.) KUWANA Yoshihisa 1064-8, Shimotogari, Nagaizumi-cho, Sunto-gun, Shizuoka 411-0943 Japan inventor only (If this check-box is marked, do not fill in below.)								
State (that is, country) of nationality: JP	State (that is, country) o	f residence: JP						
This person is applicant all designated for the purposes of:		e United States the States indicated in the Supplemental Box						
Further applicants and/or (further) inventors are indicated o	n another continuation she	eet.						

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Box N	No.V	DESIGNATION OF STATES								
The f	The following designations are hereby made under Rule 4.9(a) (mark the applicable check-boxes; at least one must be marked):									
1	Regional Patent									
1 _	AP ARIPO Patent: GH Ghana, GM Gambia, KE Kenya, LS Lesotho, MW Malawi, SD Sudan, SZ Swaziland, UG Uganda,									
	A.	ZW Zimbabwe, and any other State which is a Control	actin	g Stat	e of the Harare Protocol and of the PCT					
	EA	Eurasian Patent: AM Armenia, AZ Azerbaijan, BY Belarus, KG Kyrgyzstan, KZ Kazakhstan, MD Republic of Moldova, RU Russian Federation, TJ Tajikistan, TM Turkmenistan, and any other State which is a Contracting State of the Eurasian Patent Convention and of the PCT								
図	EP	European Patent: AT Austria, BE Belgium, CH a DK Denmark, ES Spain, FI Finland, FR France, GB I	Jnite	d King	itzerland and Liechtenstein, CY Cyprus, DE Germany, gdom, GR Greece, IE Ireland, IT Italy, LU Luxembourg, other State which is a Contracting State of the European					
	OA OAPI Patent: BF Burkina Faso. BJ Benin. CF Central African Republic, CG Congo, CI Côte d'Ivoire, CM Cameroon, GA Gabon, GN Guinea, ML Mali, MR Mauritania, NE Niger, SN Senegal, TD Chad, TG Togo, and any other State which is a member State of OAPI and a Contracting State of the PCT (if other kind of protection or treatment desired, specify on dotted line)									
Natio	nal Pa	atent (if other kind of protection or treatment desired,								
		Albania	Speci		Lesotho					
		Armenia			Lithuania					
		Austria			Luxembourg					
		Australia			Latvia					
		Azerbaijan			Republic of Moldova					
		Bosnia and Herzegovina			Madagascar					
		Barbados			The former Yugoslav Republic of Macedonia					
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		Georgia	X	SK						
		Ghana			Sierra Leone					
		Gambia		TJ	Tajikistan					
		Guinea-Bissau			Turkmenistan					
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Ø	HU	Hungary		TT	Trinidad and Tobago					
	ID	Indonesia	M	UA	Ukraine					
×	IL	Israel			Uganda					
	IS	Iceland	図		United States of America					
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	KE	Kenya	П	117	Uzbekistan					
		Kyrgyzstan	×		Viet Nam					
=	KP	Democratic People's Republic of Korea								
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Precautionary Designation Statement: In addition to the designations made above, the applicant also makes under Rule 4.9(b) all other designations which would be permitted under the PCT except any designation(s) indicated in the Supplemental Box as being excluded from the scope of this statement. The applicant declares that those additional designations are subject to confirmation and that any designation which is not confirmed before the expiration of 15 months from the priority date is to be regarded as withdrawn by the applicant at the expiration of that time limit. (Confirmation of a designation consists of the filing of a notice specifying that designation and the payment of the designation and confirmation fees. Confirmation must reach the receiving Office within the 15-month time limit.)

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Sheet No.	4 ·

Filing date of carlier application (daty/month/year) Item (1)	Box No. VI PRIORITY	CLAIM		Further prio	rity claims are indicated	in the Supplemental Box.		
of earlier application (adoptionship part) Item (1)	Filing date		Number					
Section Patent Application Patent Pate	of earlier application	of ear	lier application		regional application:*	international application:		
item (2) Item (3) Item (4) Item (
The receiving Office is coquested to prepare and transmit to the International Bureau a certified copy of the earlier application () (onto 1) if the earlier application was filed with the Office which for the purposes of the present international application is the receiving Office) identified above as item(s): (1)	item (2)							
Control of the carlier application(s) (only if the earlier application was filed with the Office which for the purposes of the present international application is the receiving Office identified above as item(s): Where the earlier application is an ARPO application, it is mandatory to indicate in the Supplemental Box are least one country party to the Pack Convention for the Protection of mulastrale Protection of mulastrale Protection of mulastrale Protection and are least one country party to the Pack Convention for the Protection of mulastrale Protection and are least one country party to the Pack Convention for the Protection of mulastrale Protection was filed (Rule 4-10(b)(iii)). See Supplemental Box. Box No. VII INTERNATIONAL SEARCHING AUTHORITY	item (3)							
Convenion for the Protection of Industrial Property for which that earlier application was filed (Rule 4.10fs)(file). See Supplemental Bax. Box No. VII International Searching Authorities are the Authority chosen: the two-letter code may be used): Date (day/month/year) Number Country (or regional Office to the Authority chosen: the two-letter code may be used): Date (day/month/year) Number Country (or regional Office to the following number of sheets: 1. Search has been carried out by or requested from the International Searching Authorities are the Authority chosen: the two-letter code may be used): Date (day/month/year) Number Country (or regional Office to the Authority chosen: the two-letter code may be used): Date (day/month/year) Number Country (or regional Office to the Authority chosen: the two-letter code may be used): Date (day/month/year) Number Country (or regional Office to the Authority chosen: the two-letter code may be used): Date (day/month/year) Number Country (or regional Office to the Authority chosen: the two-letter code may be used): Date (day/month/year) Number Country (or regional Office to the Authority chosen: the two-letter code may be used): Date (day/month/year) Number Country (or regional Office to the Country (or regional Office Country (or regi	of the earlier application	n(s) (only i)	the earlier applic	cation was filed with the	Office which for the	(1)		
Choice of International Searching Authority (ISA) (If two or more international Searching Authorities are started in the Authority chosen: the two-letter code may be used): ISA / JP Box No. VIII CHECK LIST; LANGUAGE OF FILING This international application contains the following number of sheets: request is 4 description (excluding sequence listing part): 1.	* Where the earlier application Convention for the Protection o	is an ARIPC f Industrial H	application, it is more repetty for which the	andatory to indicate in the S hat earlier application was fit	upplemental Box at least of led (Rule 4.10(b)(ii)). See	one country party to the Paris Supplemental Box.		
(if two or more international Searching Authorities are competent to carry out the international search, indicate the Authority chosen; the two-letter code may be used): ISA / JP Box No. VIII CHECK LIST; LANGUAGE OF FILING This international application contains the following number of sheets: request 4	Box No. VII INTERNAT	IONAL SE	ARCHING AUT	HORITY	· · · · · · · · · · · · · · · · · · ·			
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of description 0 8. nucleotide and/or amino acid sequence listing in computer readable form Total number of sheets 19 9. other (specify): Request for transmittal of priority document Figure of the drawings which should accompany the abstract: Language of filing of the international application: Box No. IX SIGNATURE OF APPLICANT OR AGENT Next to each signature, indicate the name of the person signing and the capacity in which the person signs (if such capacity is not obvious from reading the request Kyowa Hakko Kogyo Co., Ltd. KUROKAWA Masako SUZUKI Fumio SHIMADA Junichi IKEDA Ken KUWANA Yoshihisa 1. Date of actual receipt of the purported international application: 3. Corrected date of actual receipt due to later but timely received papers or drawings completing the purported international application: 4. Date of timely receipt of the required corrections under PCT Article 11(2): 5. International Searching Authority 18A / Up 6. Transmittal of search copy delayed	drawings :	0	6. 🔲 translatio	n of international applicati	on into (language):			
Total number of sheets 19 9 other (specify): Request for transmittal of priority document Figure of the drawings which should accompany the abstract: Box No. IX SIGNATURE OF APPLICANT OR AGENT Next to each signature, indicate the name of the person signing and the capacity in which the person signs (if such capacity is not obvious from reading the request Kyowa Hakko Kogyo Co., Ltd. KUROKAWA Masako SUZUKI Fumio SHIMADA Junichi IKEDA Ken KUWANA Yoshihisa 1. Date of actual receipt of the purported international application: 3. Corrected date of actual receipt due to later but timely received papers or drawings completing the purported international application: 4. Date of timely receipt of the required corrections under PCT Article 11(2): 5. International Searching Authority ISA (ID) 6. Transmittal of search copy delayed		0		• .	_	•		
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Kyowa Hakko Kogyo Co., Ltd. KUROKAWA Masako SUZUKI Fumio SHIMADA Junichi IKEDA Ken KUWANA Yoshihisa For receiving Office use only 1. Date of actual receipt of the purported international application: 3. Corrected date of actual receipt due to later but timely received papers or drawings completing the purported international application: 4. Date of timely receipt of the required corrections under PCT Article 11(2): 5. International Searching Authority ISA / ID 6. Transmittal of search copy delayed	Box No. IX SIGNATUR	E OF APP	LICANT OR AG	ENT				
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by the International Bureau:

Form PCT/RO/101 (last sheet) (July 1998)

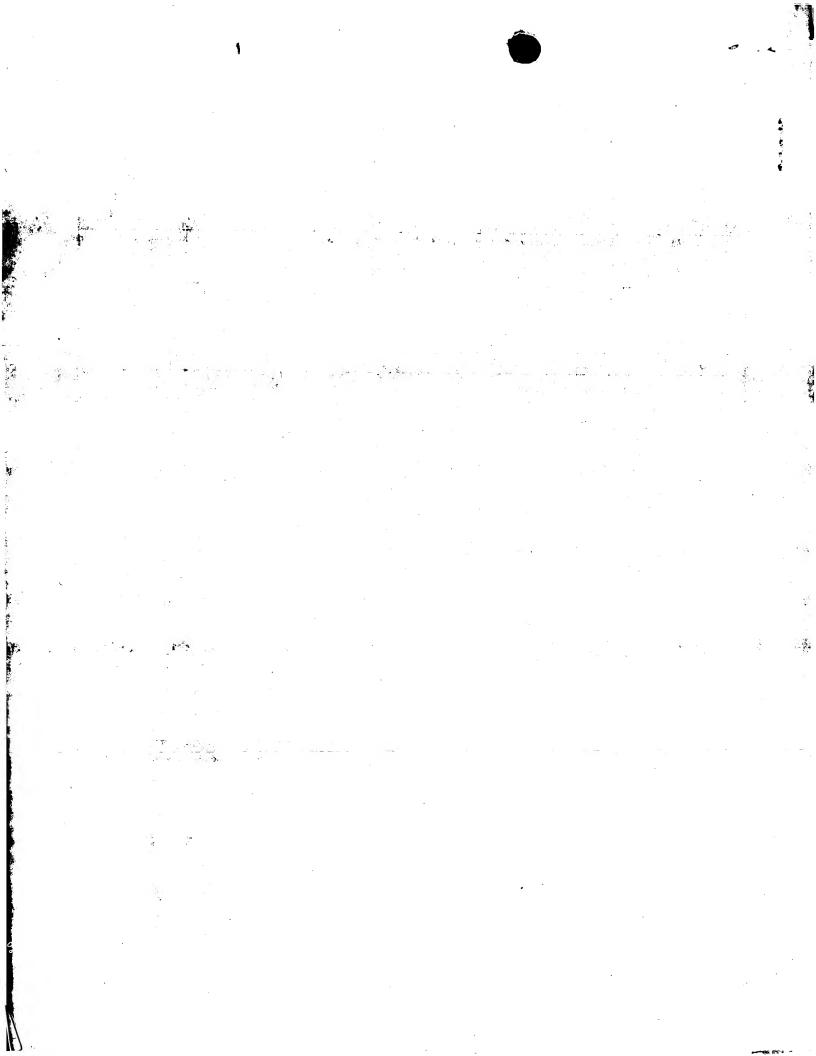
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INTERNATIONAL SEARCH REPORT

International application No.
PCT/JP98/03980

A. CLASS	IFICATION OF SUBJECT MATTER C1 A61K31/52 // C07D473/04, C	07D473/20, C07D473/22	
According to	International Patent Classification (IPC) or to both nat	tional classification and IPC	
B. FIELDS	SEARCHED		
Int.	ocumentation searched (classification system followed local A61K31/52, C07D473/04, C07	7D473/20, C07D4/3/22	
	ion searched other than minimum documentation to the	·	
Electronic da CApl	ata base consulted during the international search (namus (STN), REGISTRY (STN)	ne of data base and, where practicable, so	earch terms used)
C. DOCU	MENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where app	propriate, of the relevant passages	Relevant to claim No.
Х	JP, 2613355, B2 (Kyowa Hakko 27 February, 1997 (27. 02. 9° & EP, 590919, A1 & NO, 9303 & CA, 2107014, A & US, 5484 & US, 5587378, A & BR, 1100	7) 3452, A 4920, A	1-3, 5
х	JP, 2613352, B2 (Kyowa Hakko 27 February, 1997 (27. 02. 9 & EP, 565377, A1 & NO, 930 & CA, 2093403, A & US, 548 & US, 5587378, A & DE, 693 & ES, 2112386, T3 & BR, 110	7) 1317, A 4920, A 16067, E	1-3, 5
х	JP, 6-239862, A (Kyowa Hakko 30 August, 1994 (30. 08. 94) & ER, 607607, A1 & NO, 930 & CA, 2112031, A & DE, 693 & US, 5670498, A	4792, A	1-3, 5
× Furthe	er documents are listed in the continuation of Box C.	See patent family annex.	
* Special "A" docum conside "E" earlier "L" docum cited to special "O" docum means "P" docum	I categories of cited documents: ent defining the general state of the art which is not cred to be of particular relevance document but published on or after the international filing date ent which may throw doubts on priority claim(s) or which is establish the publication date of another citation or other reason (as specified) ent referring to an oral disclosure, use, exhibition or other ent published prior to the international filing date but later than ority date claimed	"T" later document published after the inte date and not in conflict with the applic the principle or theory underlying the document of particular relevance; the considered novel or cannot be considered when the document is taken alone document of particular relevance; the considered to involve an inventive ster combined with one or more other such being obvious to a person skilled in the document member of the same patent."	ation but cited to understand invention claimed invention cannot be red to involve an inventive step claimed invention cannot be to when the document is documents, such combination e art family
	actual completion of the international search November, 1998 (25. 11. 98)	Date of mailing of the international se 8 December, 1998	arch report (08. 12. 98)
Name and r	nailing address of the ISA/ anese Patent Office	Authorized officer	
Faccimile N	Vo.	Telephone No.	



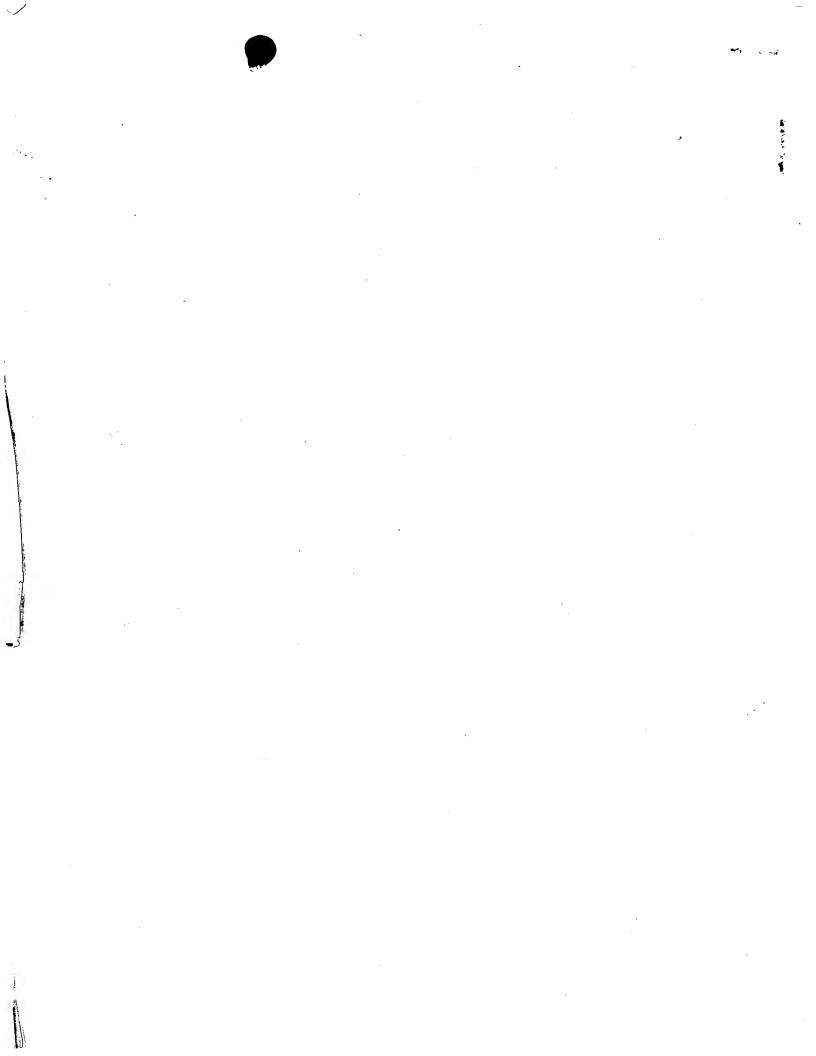


INTERNATIONAL SEARCH REPORT



International application No.
PCT/JP98/03980

ategory*	Citation of document, with indication, where appropriate, of the	relevant passages	Relevant to claim No
X	JP, 6-47539, B2 (Adir et Co.), 22 June, 1994 (22. 06. 94) & EP, 470317, A & FR, 2665636, A & PT, 95467, A & AU, 9063228, A & US, 5173491, A & DE, 69008853, E & ES, 2056415, T3 & IE, 65158, B & CA, 2026118, A	Olovani passiges	1-3, 5
х	US, 4772607, A (Warner-Lambert Company 20 September, 1988 (20. 09. 88) (Fami	y), ly: none)	1-3, 5
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今後の手続きについては、国際調査報告の送付通知様式(PCT/ISA/220)

🗴 なし



EP

出願人又は代理人



国際調査報告

(法8条、法施行規則第40、41条) [PCT18条、PCT規則43、44]

の書類記号 1082		及で	び下記5を	参照すること。
国際出願番号 PCT/JP98/03980	国際出願日 (日.月.年)	04.09.		優先日 (日.月.年) 05.09.97
出願人 (氏名又は名称) 協和 醱 酵工業	连株式会社			,
	,			
国際調査機関が作成したこの国際調査 この写しは国際事務局にも送付される		則第41条(P (CT18条	の規定に従い出願人に送付する。
この国際調査報告は、全部で 4	ページである。	5		
この調査報告に引用された先行	技術文献の写しも?	添付されている	5.	
1. x 請求の範囲の一部の調査が	ぶできない(第1	欄参照)。		,
2. 第明の単一性が欠如してい	ヽる(第Ⅱ欄参照)) .		•
3. □ この国際出願は、ヌクレス 査を行った。	チド及び/又は、	アミノ酸配列!	リストを含ん	んでおり、次の配列リストに基づき国際調
□ この国際出願と共に提出	されたもの		٠	-
出願人がこの国際出願と	は別に提出した。	もの		•
□ しかし、出願時のほ	際出願の開示の	範囲を越える事	事項を含まれ	ない旨を記載した書面が添付されていない
この国際調査機関が書格	きえたもの			
				,
4. 発明の名称は x 出願 	[人が提出したもの	のを承認する。		
□ 次に	示すように国際記	調査機関が作成	戈した。	·
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5. 要約は 🗴 出願	(人が提出したもの	のを承認する。		
国際	欄に示されている 調査機関が作成し 際調査機関に意見	した。出願人に	は、この国際	7条(PCT規則38.2(b))の規定により 際調査報告の発送の日から1カ月以内にこ 5。

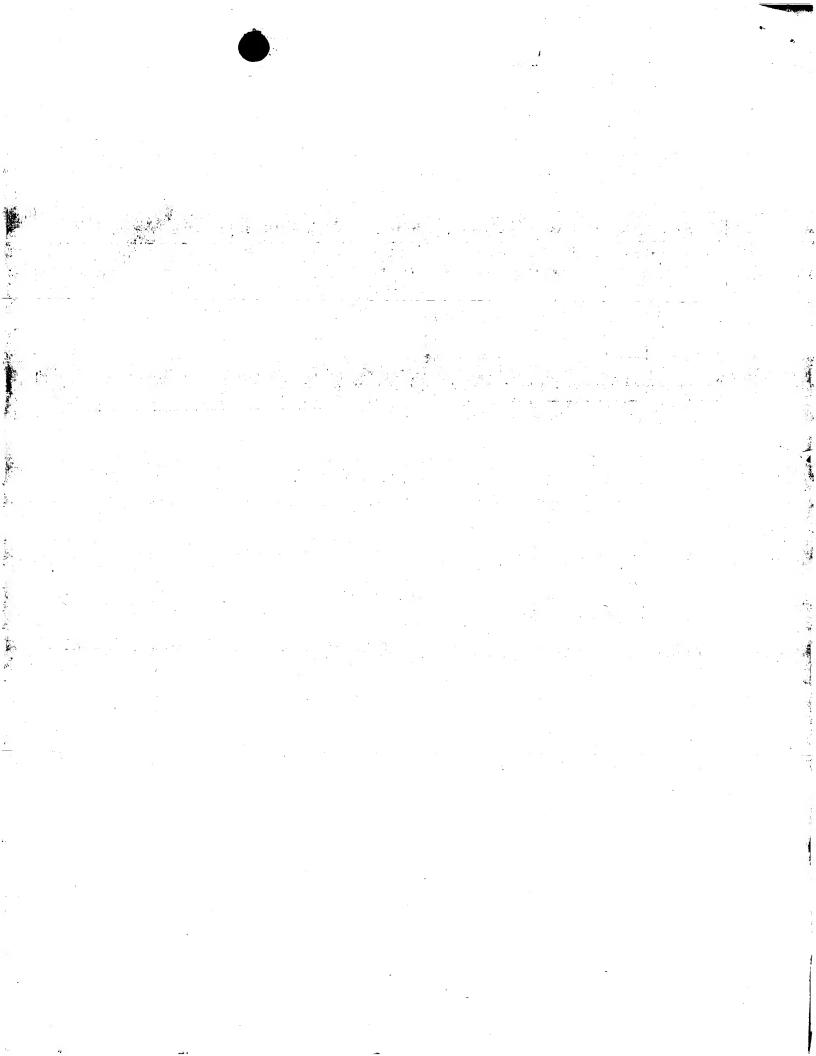
様式PCT/ISA/210 (第1ページ) (1992年7月).

第 ______図とする。 □ 出願人が示したとおりである。

□ 出願人は図を示さなかった。

□ 本図は発明の特徴を一層よく表している。

6. 要約書とともに公表される図は、





国際出願番 PCT/JP98/03980

第[欄	請求の範囲の一部の調査ができないときの意見(第1ページの1の続き)
法第8名 成しなる	条第3項(PCT17条(2)(a))の規定により、この国際調査報告は次の理由により請求の範囲の一部について作 かった。
1. x	請求の範囲は、この国際調査機関が調査をすることを要しない対象に係るものである。 つまり、
	請求の範囲4は、人の治療による処置方法の発明に該当する。
2.	請求の範囲は、有意義な国際調査をすることができる程度まで所定の要件を満たしていない国際出願の部分に係るものである。つまり、
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3.	請求の範囲は、従属請求の範囲であってPCT規則6.4(a)の第2文及び第3文の規定に 従って記載されていない。
第Ⅱ欄	発明の単一性が欠如しているときの意見 (第1ページの2の続き)
次に过	Lべるようにこの国際出願に二以上の発明があるとこの国際調査機関は認めた。
•	
1.	出願人が必要な追加調査手数料をすべて期間内に納付したので、この国際調査報告は、すべての調査可能な請求
	の範囲について作成した。
2. 📙	追加調査手数料を要求するまでもなく、すべての調査可能な請求の範囲について調査することができたので、追 加調査手数料の納付を求めなかった。
3.	出願人が必要な追加調査手数料を一部のみしか期間内に納付しなかったので、この国際調査報告は、手数料の納付のあった次の請求の範囲のみについて作成した。
4.	出願人が必要な追加調査手数料を期間内に納付しなかったので、この国際調査報告は、請求の範囲の最初に記載されている発明に係る次の請求の範囲について作成した。
追加調査	手数料の異議の申立てに関する注意 〕 追加調査手数料の納付と共に出願人から異議申立てがあった。

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Α.	発明の属する分野の分類	(国際特許分類	(IPC)
4 1 .			(1 1 0)

Int. Cl⁶ A 6 1 K 3 1 / 5 2 // C 0 7 D 4 7 3 / 0 4, C 0 7 D 4 7 3 / 2 0, C 0 7 D 4 7 3 / 2 2

B. 調査を行った分野

調査を行った最小限資料(国際特許分類(IPC))

Int. Cl⁶ A 6 1 K 3 1/52, C 0 7 D 4 7 3/04, C 0 7 D 4 7 3/20, C 0 7 D 4 7 3/22

最小限資料以外の資料で調査を行った分野に含まれるもの

国際調査で使用した電子データベース (データベースの名称、調査に使用した用語)

CAplus (STN), REGISTRY (STN)

C. 関連する	ると認められる文献 しゅうしゅう しゅうしゅう しゅうしゅう	
引用文献の カテゴリー*	引用文献名 及び一部の箇所が関連するときは、その関連する箇所の表示	関連する 請求の範囲の番号
X	JP, 2613355, B2 (協和醱酵工業株式会社) 27.2月.1997(27.02.97) & EP, 590919, A1 & NO, 9303452, A & CA, 2107014, A & US, 5484920, A & US, 5587378, A & BR, 1100971, A3	1-3, 5
X	JP, 2613352, B2 (協和醱酵工業株式会社) 27. 2月. 1997 (27. 02. 97) & EP, 565377, A1 & NO, 9301317, A & CA, 2093403, A & US, 5484920, A & US, 5587378, A & DE, 69316067, E & ES, 2112386, T3 & BR, 1100636, A3	1-3, 5
x	JP,6-239862,A(協和醱酵工業株式会社)30.8月.1994(30.08.94) & EP,607607,A1 & NO,9304792,A & CA,2112031,A	1-3, 5

|x| C欄の続きにも文献が列挙されている。

□ パテントファミリーに関する別紙を参照。

- * 引用文献のカテゴリー
- 「A」特に関連のある文献ではなく、一般的技術水準を示す もの
- 「E」先行文献ではあるが、国際出願日以後に公表されたも の
- 「L」優先権主張に疑義を提起する文献又は他の文献の発行 日若しくは他の特別な理由を確立するために引用する 文献(理由を付す)
- 「O」ロ頭による開示、使用、展示等に言及する文献
- 「P」国際出願目前で、かつ優先権の主張の基礎となる出願

- の日の後に公表された文献
- 「T」国際出願日又は優先日後に公表された文献であって て出願と矛盾するものではなく、発明の原理又は理 論の理解のために引用するもの
- 「X」特に関連のある文献であって、当該文献のみで発明 の新規性又は進歩性がないと考えられるもの
- 「Y」特に関連のある文献であって、当該文献と他の1以 上の文献との、当業者にとって自明である組合せに よって進歩性がないと考えられるもの
- 「&」同一パテントファミリー文献

国際調査を完了した日

25.11.98

& DE, 69304883, E & US, 5670498, A

国際調査報告の発送日

08,12,98

国際調査機関の名称及びあて先

日本国特許庁 (ISA/JP) 郵便番号100-8915

東京都千代田区霞が関三丁目4番3号

特許庁審査官(権限のある職員) 中木 亜希 # 4C 9282

電話番号 03-3581-1101 内線 3454

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国際調	5

	C (続き).	関連すると認められる文献				
	引用文献の カテゴリー*	引用文献名 及び一部の箇所が関連するときは、その関連する箇所の表示	関連する 請求の範囲の番号			
	Х	JP, 6-47539, B2 (アディール ェ コンパ゚=-) 22.6月.1994(22.06.94) & EP, 470317, A & FR, 2665636, A & PT, 95467, A & AU, 9063228, A & US, 5173491, A & DE, 69008853, E & ES, 2056415, T3 & IE, 65158, B & CA, 2026118, A	1-3, 5			
	X	US,4772607,A (Warner-Lambert Company)20.9月.1988(20.09.88) (ファミリーなし)	1-3, 5			
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UNITED STATES PATENT AND TRADEMARK OFFICE CERTIFICATE OF CORRECTION

PATENT NO. :

4,772,607

DATED

September 20, 1988

INVENTOR(S) :

Edward W. Badger, et al

It is certified that error appears in the above—identified patent and that said Letters Patent is hereby corrected as shown below:

In column 16 line 2 change " $S(0)_R$ " to -- $S(0)_k$ --.

In column 16 line 5 change "NH(CH₂)₂₆" to --NH(CH₂)₂₋₆--.

Signed and Sealed this Fourteenth Day of February, 1989

Attest:

DONALD J. QUIGG

Attesting Officer

Commissioner of Patents and Trademarks

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世界知的所有権機関 事 務 局 午協力条約に基づいて公開された国際出願



(51) 国際特許分類6

A61K 31/52 // C07D 473/04, 473/20,

A1

(11) 国際公開番号

WO99/12546

(43) 国際公開日

1999年3月18日(18.03.99)

(21) 国際出願番号

PCT/JP98/03980

(22) 国際出願日

1998年9月4日(04.09.98)

(30) 優先権データ

特願平9/240565

1997年9月5日(05.09.97)

JP

(71) 出願人 (米国を除くすべての指定国について) 協和嚴酵工業株式会社

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(75) 発明者/出願人(米国についてのみ)

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〒411-0943 静岡県駿東郡長泉町下土狩1064-8 Shizuoka, (JP)

(81) 指定国 AU, BG, BR, BY, CN, CZ, HU, IL, JP, KR, MX, NO, NZ, PL, RO, SG, SI, SK, UA, US, VN, ユーラシア特許 (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), 欧州特許 (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE).

添付公開書類

国際調査報告書

REMEDIAL AGENT FOR NEURAL DEGENERATION (54)Title:

(54)発明の名称 神経変性疾患治療剤

(57) Abstract

A remedy for neural degeneration which contains a xanthine derivative represented by general formula (I) or a pharmacologically acceptable salt thereof as the active ingredient.

$$\begin{array}{c|c}
X^2 & R^3 \\
 & N & R^4 \\
 & N & R^4
\end{array}$$

$$\begin{array}{c|c}
X^1 & N & R^4 \\
 & R^2 & R^4
\end{array}$$

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P.B.5818 - Patentlaan 2 2280 HV Rijswijk (ZH) 2 +31 70 340 2040 TX 31651 epo nl FAX +31 70 340 3016 Europäisches Patentamt

Zweigstelle in Den Haag Recherchenabteilung European Patent Office

Branch at The Hague Search division Offic européen des br vets

Département à La Haye Division de la recherche

VOSSIUS & PARTNER Siebertstrasse 4 81675 München ALLEMAGNE

EINGEGANGEN Vossius & Partner 18. Nov. 2002

Datum/Date

15.11.02

Zeichen/Ref./Réf. E1324EP

Anmeldung Nr./Application No./Demande n°./Patent Nr./Patent No./Brevet n°.

98941725.8-1216-JP9803980

Anmelder/Applicant/Demandeur/Patentinhaber/Proprietor/Titulaire
KYOWA HAKKO KOGYO CO., LTD.

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COMMUNICATION

The European Patent Office herewith transmits as an enclosure the European search report for the above-mentioned European patent application.

If applicable, copies of the documents cited in the European search report are attached.

Additional set(s) of copies of the documents cited in the European search report is (are) enclosed as well.

REFUND OF THE SEARCH FEE

If applicable under Article 10 Rules relating to fees, a separate communication from the Receiving Section on the refund of the search fee will be sent later.





SUPPLEMENTARY PARTIAL EUROPEAN SEARCH REPORT

Application Number

which under Rule 45 of the European Patent ConventionEP 98 94 1725 shall be considered, for the purposes of subsequent proceedings, as the European search report

	DOCUMENTS CONSIDE	RED TO BE RELEVANT	-	
Category	Citation of document with in- of relevant passa	dication, where appropriate,	Relevant to claim	CLASSIFICATION OF THE APPLICATION (Int.CI.6)
X	expression in rat madenosine A2a-recept NEUROSCIENCE LETTERS vol. 231, no. 2,	S. IRELAND 8 AUG 1997, -08-08), pages 83-86,	1-3	A61K31/52 C07D473/04 //(C07D473/04, 473:20,473:22)
X	EP 0 607 607 A (KYO) 27 July 1994 (1994-0) * figure I * * page 1, line 1 - * page 11, line 1 - * page 11 - page 15 1-3,6,9-14,16,17,20- * claims 1-11 *	07-27) line 9 * page 15, line 33 *	1-3	·
		-/		TECHNICAL FIELDS SEARCHED (Int.Cl.6)
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The Sear not comp be carried Claims se Claims se Claims no Reason fr	nd available at the start of the sear MPLETE SEARCH ch Division considers that the present a	application, or some or all of its claims, does/ a meaningful search into the state of the art o	do	
	Place of search	Date of completion of the search		Examiner
	THE HAGUE	6 November 2002	Str	ack, E
X : par Y : par doc A : ted O : nor	ATEGORY OF CITED DOCUMENTS ticularly relevant if taken alone ticularly relevant if combined with anoth ument of the same category nnological background n-written disclosure transmissions and the comment of the commen	L : document cited for	cument, but pub te n the application or other reasons	lished on, or

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Application Number

	DOCUMENTS CONSIDERED TO BE RELEVANT	CLASSIFICATION OF THE APPLICATION (Int.Cl.6)	
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	
X	EP 0 565 377 A (KYOWA HAKKO KOGYO KK) 13 October 1993 (1993-10-13) * page 2, line 1 - line 2 * * claims 1-9 * in particular examples 1, 2, 4 and 17 * page 12 - page 15; table 2 *	1-3	
X	EP 0 590 919 A (KYOWA HAKKO KOGYO KK) 6 April 1994 (1994-04-06) * page 3, line 1 - line 6 * * page 11-17; table 1 * * claims 1-22 *	1-3	
X,D	EP 0 698 607 A (KYOWA HAKKO KOGYO KK) 28 February 1996 (1996-02-28) * page 1, line 5 - line 8 * * page 6 - page 8; table 1 * * claims 1-12 *	1-3	TECHNICAL FIELDS SEARCHED (Int.Cl.6)
X	DE 42 36 331 A (BOEHRINGER INGELHEIM KG) 5 May 1994 (1994-05-05) * claims 2,6 *	1,2	
X	CANHAO P ET AL: "1,3-DIPROPYL-8-CYCLOPENTYLXANTHINE ATTENUATES THE NMDA RESPONSE TO HYPOXIA IN THE RAT HIPPOCAMPUS" BRAIN RESEARCH, AMSTERDAM, NL, vol. 1/2, no. 661, 1994, pages 265-273, XPO08004873 ISSN: 0006-8993 * abstract *	1,2	
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Application/Number

[DOCUMENTS CONSIDERED TO BE RELEVANT	CLASSIFICATION OF THE APPLICATION (Int.CI.6)	
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	
X	LUBITZ VON D K J E ET AL: "CHRONIC ADMINISTRATION OF SELECTIVE ADENOSINE A1 RECEPTOR AGONIST OR ANTAGONIST IN CEREBRAL ISCHEMIA" EUROPEAN JOURNAL OF PHARMACOLOGY, AMSTERDAM, NL, vol. 2, no. 256, 21 April 1994 (1994-04-21), pages 161-167, XP008004867 ISSN: 0014-2999 * abstract *	1,2	
x	PHILLIS J W: "THE EFFECTS OF SELECTIVE A1 AND A2A ADENOSINE RECEPTOR ANTAGONIST ON CEREBRAL ISHCEMIC INJURY IN THE GERBIL" BRAIN RESEARCH, AMSTERDAM, NL, vol. 705, no. 1/2, 24 December 1995 (1995-12-24), pages 79-84, XP001006295 ISSN: 0006-8993 * abstract *	1-3	TECHNICAL FIELDS SEARCHED (Int.Cl.6)
X	MACGREGOR D G ET AL: "BLOCKADE BY 1,3-DIPROPYL-8-CYCLOPENTYLXANTHINE (CPX) OF PURINE PROTECTION AGAINST KAINATE NEUROTOXICITY" BRAIN RESEARCH, AMSTERDAM, NL, vol. 644, no. 2, 1994, pages 339-342, XP001006257 ISSN: 0006-8993 * abstract *	1,2	·
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Application Number

	DOCUMENTS CONSIDERED TO BE RELEVANT	CLASSIFICATION OF THE APPLICATION (Int.CI.6)	
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	
X	EP 0 374 808 A (BOEHRINGER INGELHEIM KG; BOEHRINGER INGELHEIM INT (DE)) 27 June 1990 (1990-06-27) * page 5, line 55 - page 6, line 11 * * page 2, line 1 - line 15 * * page 22 - page 29; examples 25-30,32-51,54-78; table I *	1,2	
X	US 5 173 491 A (DUHAULT JACQUES ET AL) 22 December 1992 (1992-12-22) * column 1, line 1 - column 2, line 15 *	1,2	
X	EP 0 389 282 A (BEECHAM WUELFING GMBH & CO KG; BEECHAM GROUP PLC (GB)) 26 September 1990 (1990-09-26) * page 3, line 12 - line 17 * * claims 1,15 *	1,2	TECHNICAL FIELDS SEARCHED (Int.CI.6)
Y .	DALPIAZ A ET AL: "DE NOVO ANALYSIS OF RECEPTOR BINDING AFFINITY DATA OF 8-ETHENYL-XANTHINE ANTAGONISTS TO ADENOSINE A1 AND A2A RECEPTORS" ARZNEIMITTEL FORSCHUNG. DRUG RESEARCH, EDITIO CANTOR. AULENDORF, DE, vol. 5, no. 47, 1997, pages 591-594, XP001073979 ISSN: 0004-4172 * abstract * * tables 1,2 * conclusions * page 594 *	1-3	
	-/		*



Application Number

	DOCUMENTS CONSIDERED TO BE RELEVANT	APPLICATION (Int.CI.6)	
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	
Y	DATABASE MEDLINE 'Online! 1996 MALLY J ET AL: "Potential role of adenosine antagonist therapy in pathological tremor disorders." Database accession no. NLM9364577 XP002205263 * abstract * & PHARMACOLOGY & THERAPEUTICS. ENGLAND 1996, vol. 72, no. 3, 1996, pages 243-250, ISSN: 0163-7258	1-3	
Ρ,Χ	KANDA T ET AL: "ADENOSINE A2A RECEPTORS MODIFY MOTOR FUNCTION IN MPTP-TREATED COMMON MARMOSETS" NEUROREPORT, RAPID COMMUNICATIONS OF OXFORD, OXFORD, GB, vol. 9, no. 12, 24 August 1998 (1998-08-24), pages 2857-2860, XP001006279 ISSN: 0959-4965 * abstract * conclusion * page 2860 *	1-3	TECHNICAL FIELDS SEARCHED (Int.Cl.6)
P,X	KANDA T ET AL: "ADENOSINE A2A ANTAGONIST: A NOVEL ANTIPARKINSONIAN AGENT THAT DOES NOT PROVOKE DYSKINESIA IN PARKINSONIAN MONKEYS" ANNALS OF NEUROLOGY, BOSTON, US, vol. 4, no. 43, 1998, pages 507-513, XP008004872 ISSN: 0364-5134 * abstract * * page 508, column 2, paragraph 3 * * page 512, column 2, paragraph 3 - paragraph 4 *	1-3	



INCOMPLETE SEARCH SHEET C

Application Number

EP 98 94 1725

Claim(s) searched incompletely: 1-3

Reason for the limitation of the search:

Present claims 1-3 relate to an extremely large number of possible compounds. Support within the meaning of Article 84 EPC and disclosure within the meaning of Article 83 EPC is to be found, however, for only a very small proportion of the compounds claimed. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible.

Furthermore, present claims 1-3 relate to pathological conditions referred to as "neurodegenerative disorders" as the characterising feature. Based upon information readily available, the skilled person would not be aware of all the pathologies possibly involving neurodegeneration. The use of this expression in the present context is considered to lead to a lack of clarity within the meaning of Article 84 EPC. It is not fully possible to determine the diseases for which protection might legitimately be sought. The lack of clarity is such as to render a meaningful complete search impossible.

Consequently, the search has been carried out for those parts of the claims which appear to be supported and disclosed, namely those parts relating to the use of compounds 1-4 of the examples in relation to the treatment of neurodegenerative disorders as listed on page 13, lines 2-6 of the description, with due regard to the general idea underlying the present invention.

This annex lists the patent family members relating to the patent documents cited in the above-mentioned European search report. The members are as contained in the European Patent Office EDP file on The European Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

06-11-2002

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ANNEX TO THE EUROPEAN SEARCH REPORT ON EUROPEAN PATENT APPLICATION NO.

EP 98 94 1725

This annex lists the patent family members relating to the patent documents cited in the above—mentioned European search report. The members are as contained in the European Patent Office EDP file on The European Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

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INTERNATIONAL SEARCH REPORT

International application No. PCT/JP98/03980

A. CLASS Int.	A. CLASSIFICATION OF SUBJECT MATTER Int.Cl ⁶ A61K31/52 // C07D473/04, C07D473/20, C07D473/22								
According to International Patent Classification (IPC) or to both national classification and IPC									
B. FIELDS	S SEARCHED								
Int.	Minimum documentation searched (classification system followed by classification symbols) Int.Cl ⁶ A61K31/52, C07D473/04, C07D473/20, C07D473/22								
Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched									
Electronic d CApl	ata base consulted during the international search (name us (STN), REGISTRY (STN)	ne of data base and, where practicable, s	earch terms used)						
C. DOCU	MENTS CONSIDERED TO BE RELEVANT								
Category*	Citation of document, with indication, where app	propriate, of the relevant passages	Relevant to claim No.						
х	JP, 2613355, B2 (Kyowa Hakko 27 February, 1997 (27. 02. 97 & EP, 590919, A1 & NO, 9303 & CA, 2107014, A & US, 5484 & US, 5587378, A & BR, 1100	7) 3452, A 4920, A	1-3, 5						
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× Furth	er documents are listed in the continuation of Box C.	See patent family annex.							
"A" docum conside "E" earlier "L" docum cited to special "O" docum means "P" docum	categories of cited documents: nent defining the general state of the art which is not ered to be of particular relevance document but published on or after the international filing date nent which may throw doubts on priority claim(s) or which is o establish the publication date of another citation or other I reason (as specified) nent referring to an oral disclosure, use, exhibition or other ent published prior to the international filing date but later than lority date claimed	"T" later document published after the interdate and not in conflict with the application the principle or theory underlying the importance of particular relevance; the considered novel or cannot be considered when the document is taken alone document of particular relevance; the considered to involve an inventive step combined with one or more other such being obvious to a person skilled in the document member of the same patent."	ation but cited to understand invention claimed invention cannot be red to involve an inventive step claimed invention cannot be to when the document is a documents, such combination e art						
	actual completion of the international search November, 1998 (25. 11. 98)	Date of mailing of the international se 8 December, 1998	arch report (08. 12. 98)						
	mailing address of the ISA/ anese Patent Office	Authorized officer							
Facsimile !	No.	Telephone No.							

INTERNATIONAL SEARCH REPORT

International application No.
PCT/JP98/03980

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Х	JP, 6-47539, B2 (Adir et Co.), 22 June, 1994 (22. 06. 94) & EP, 470317, A & FR, 2665636, A & PT, 95467, A & AU, 9063228, A & US, 5173491, A & DE, 69008853, E & ES, 2056415, T3 & IE, 65158, B & CA, 2026118, A	1-3, 5
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Form PCT/ISA/210 (continuation of second sheet) (July 1992)

A. 発明の属する分野の分類(国際特許分類(IPC))

Int. Cl⁸ A 6 1 K 3 1 / 5 2 // C 0 7 D 4 7 3 / 0 4, C 0 7 D 4 7 3 / 2 0, C 0 7 D 4 7 3 / 2 2

B. 調査を行った分野

調査を行った最小限資料(国際特許分類(IPC))

Int. Cl A 6 1 K 3 1 / 5 2, C 0 7 D 4 7 3 / 0 4, C 0 7 D 4 7 3 / 2 0, C 0 7 D 4 7 3 / 2 2

最小限資料以外の資料で調査を行った分野に含まれるもの

国際調査で使用した電子データベース (データベースの名称、調査に使用した用語)

CAplus (STN), REGISTRY (STN)

C. 関連すると認められる文献

し	3 こ 記 の り れ る 文 服	
引用文献の カテゴリー*	引用文献名 及び一部の箇所が関連するときは、その関連する箇所の表示	関連する 請求の範囲の番号
Х	JP, 2613355, B2 (協和醱酵工業株式会社) 27. 2月. 1997 (27. 02. 97) & EP, 590919, A1 & NO, 9303452, A & CA, 2107014, A & US, 5484920, A & US, 5587378, A & BR, 1100971, A3	1-3, 5
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x C欄の続きにも文献が列挙されている。

□ パテントファミリーに関する別紙を参照。

- * 引用文献のカテゴリー
- 「A」特に関連のある文献ではなく、一般的技術水準を示す もの
- 「E」先行文献ではあるが、国際出願日以後に公表されたも
- 「L」優先権主張に疑義を提起する文献又は他の文献の発行 日若しくは他の特別な理由を確立するために引用する 文献(理由を付す)
- 「O」ロ頭による開示、使用、展示等に言及する文献
- 「P」国際出願日前で、かつ優先権の主張の基礎となる出願

- の日の後に公表された文献
- 「T」国際出願日又は優先日後に公表された文献であって て出願と矛盾するものではなく、発明の原理又は理 論の理解のために引用するもの
- 「X」特に関連のある文献であって、当該文献のみで発明 の新規性又は進歩性がないと考えられるもの
- 「Y」特に関連のある文献であって、当該文献と他の1以 上の文献との、当業者にとって自明である組合せに よって進歩性がないと考えられるもの
- 「&」同一パテントファミリー文献

国際調査を完了した日

25.11.98

国際調査報告の発送日

0 8.12.98

国際調査機関の名称及びあて先

日本国特許庁(ISA/JP)

郵便番号100~8915 東京都千代田区霞が関三丁目4番3号 特許庁審査官(権限のある職員)

中木 亜希

4C | 9282

電話番号 03-3581-1101 内線 3454

国際調査報告

国際出願番号 PCT/JP98/03980

_C(続き).	関連すると認められる文献	
引用文献の カテゴリー*	引用文献名 及び一部の箇所が関連するときは、その関連する箇所の表示	関連する 請求の範囲の番号
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PATENT COOPERATION TOATY

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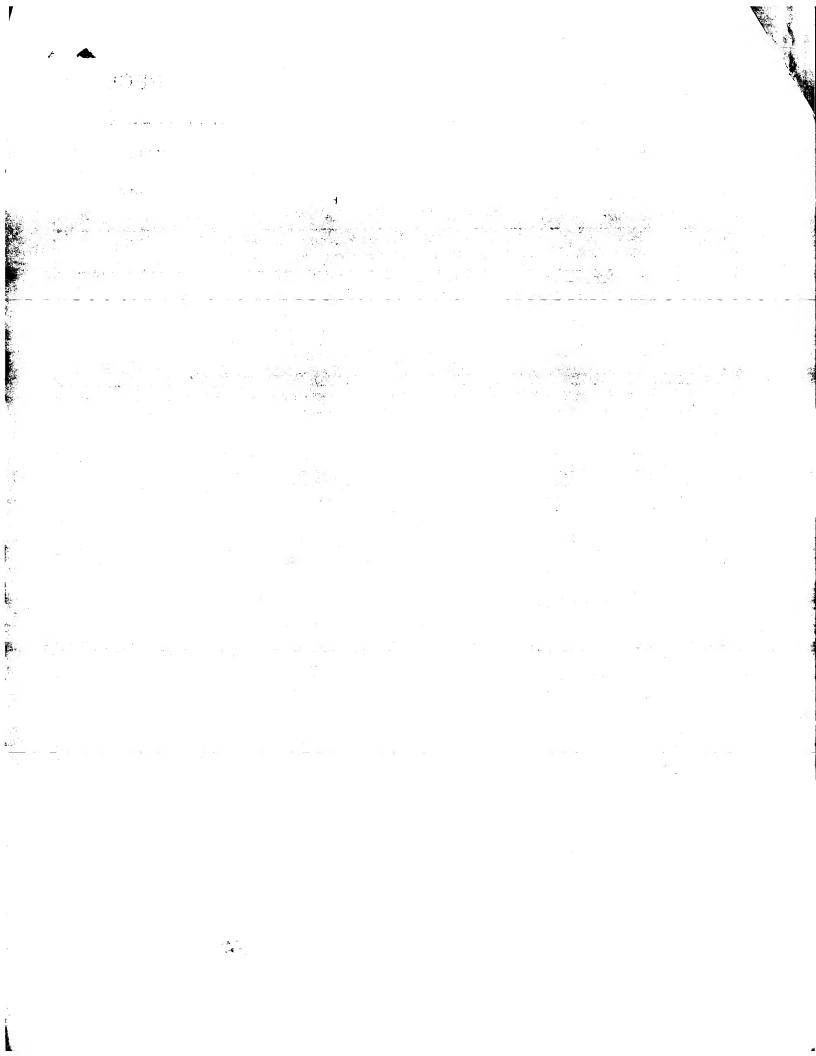
AUG 2'3 2000

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

TECH CENTER 1600/2900

Applicant's or agent's file reference	FOR FURTHER ACTION		tionofTransmittalofInternational Preliminary					
International application No.		Examination	n Report (Form PCT/IPEA/416)					
International application No. PCT/JP98/03980	International filing date (day) 04 September 1998 (04)		Priority date (day/month/year) 05 September 1997 (05.09.1997)					
International Patent Classification (IPC) or n			03 September 1997 (03.09.1997)					
A61K 31/52 // C07D 473/04, 47.								
Applicant								
KYOWA HAKKO KOGYO CO., LTD.								
 This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36. 								
2. This REPORT consists of a total of	5 sheets, includi	ng this cover s	heet.					
This report is also accompani	ed by ANNEYES is sheets	f the description	on claims and/or drawings which have been					
This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).								
These annexes consist of a total of sheets.								
3. This report contains indications relat	ing to the following items:							
Basis of the report								
II Priority								
III Non-establishment o	of opinion with regard to novelt	y, inventive ste	p and industrial applicability					
IV Lack of unity of inve	ention							
Reasoned statement	under Article 35(2) with regard	to novelty, in	ventive step or industrial applicability;					
citations and explana	ations supporting such statemer	t						
VI Certain documents of	ited							
VII Certain defects in the	e international application							
VIII Certain observations	on the international application	ı						
Date of submission of the demand	Date o	f completion of	f this report					
31 March 1999 (31.03.1	999)	27 O	ctober 1999 (27.10.1999)					
Name and mailing address of the IPEA/JP	Author	ized officer						
Japanese Patent Office, 4-3 Kasumigas Chiyoda-ku, Tokyo 100-8915, Japan								
Facsimile No.	Teleph	one No. (81-3) 3581 1101					



INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/JP98/03980

٠,

I. Basis of the report 1. With regard to the elements of the international application:* the international application as originally filed AUG 23 2000 the description: pages TECH CENTER 1,600 GT Anally filed pages , filed with the letter of , filed with the demand pages the claims: pages , as originally filed pages , as amended (together with any statement under Article 19 pages _____, filed with the demand pages _____, filed with the letter of the drawings: pages , as originally filed pages , filed with the demand ____, filed with the letter of pages the sequence listing part of the description: pages ___, as originally filed pages _____, filed with the demand pages _____, filed with the letter of 2. With regard to the language, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item. These elements were available or furnished to this Authority in the following language the language of a translation furnished for the purposes of international search (under Rule 23.1(b)). the language of publication of the international application (under Rule 48.3(b)). the language of the translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/ 3. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing: contained in the international application in written form. filed together with the international application in computer readable form. furnished subsequently to this Authority in written form. furnished subsequently to this Authority in computer readable form. The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished. The statement that the information recorded in computer readable form is identical to the written sequence listing has The amendments have resulted in the cancellation of: the description, pages ____ the claims, Nos. the drawings, sheets/fig This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).** * Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rule 70.16 ** Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.

9 · · . .

,



International application No.

PCT/JP98/03980

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability 1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of: RECEIVED the entire international application. AUG 23 2000 because: TECH CENTER 1600/2010 the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (specify): The subject matter of claim 4 relates to a method for treatment of the human body by therapy. the description, claims or drawings (indicate particular elements below) or said claims Nos. _ are so unclear that no meaningful opinion could be formed (specify): the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed. no international search report has been established for said claims Nos. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions: the written form has not been furnished or does not comply with the standard. the computer readable form has not been furnished or does not comply with the standard.

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INTERNATIONAL PRELIMINARY EXAMINATION REPORT

PCT/JP98/03980

tatement			AUG 23
Novelty (N)	Claims		YES TECH CENTER
	Claims	1-3,5	TECH CENTER NO
Inventive step (IS)	Claims		YES
	Claims	1-3,5	NO
Industrial applicability (IA)	Claims	1-3,5	YES
	Claims		NO
escribed in claim 3 of the p	07667 cribe therapeutic agents resent application as an	for Parkinson's disease, containing	
Documents 1 and 2 desertibed in claim 3 of the procument 3 describes to hibitory action against arkinson's disease. Since Parkinson's disease opamine nerve as also degeneration disease. So, documents 1-3 appregeneration diseases contains	cribe therapeutic agents resent application as an hat the compound describe haloperidol-induced is a disease based on escribed in documents ear to describe an invining the compound described described in documents	(for Parkinson's disease, containing	pplication shows for reproducing f the nigrostriatal to be a neural agent for neural application as an

Document 4 describes a therapeutic drug-composition for Alzheimer's disease, containing 1,3,7-trimethyl-8-[3-(4-dimethylaminocarbonylpiperazino)propyl]xanthine as an active ingredient, and the 1,3,7-trimethyl-8-[3-(4-dimethylaminocarbonylpiperazino)propyl]xanthine is included in the compound described in claim 2 of the present application.

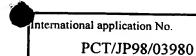
The present application (specification, page 9, lines 13-17) exemplifies Alzheimer's disease as a neural degeneration disease.

So, document 4 appears to describe an invention concerning a therapeutic agent for neural degeneration diseases containing the compound described in claim 2 of the present application as an active ingredient, and an invention concerning the use of the compound described in claim 2 of the present application for producing a therapeutic agent for neural degeneration diseases.

3) The subject matters of claims 1, 2 and 5 do not appear to involve an inventive step in view of the following document cited in the ISR.

5. US, 4772607, A

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INTERNATIONAL PRELIMINARY EXAMINATION REPORT

Supplemental Box

(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of Box V (Citations and explanations):

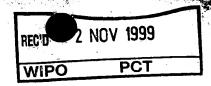
Document 5 suggests that a compound having lower alkenyl groups at the 1- and 3-positions and a cycloalkyl group at the 8-position can be used for therapy of Alzheimer's disease.

So, it could have been easily confirmed by a person skilled in the art, for example, by performing pharmacological tests, that a compound having lower alkenyl groups at the 1- and 3-positions and a cycloalkyl group at the 8-position is effective for therapy of Alzheimer's disease.

The effect achieved in the subject matters of claims 1, 2 and 5 of the present application does not appear to be at a remarkable level that cannot be anticipated by a person skilled in the art from the description of document 5.

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特許協力条約



PCT

国際予備審査報告

(法第12条、法施行規則第56条) [PCT36条及びPCT規則70]

	、又は代理人 頁記号 1082	今後の手続きについ	ては、国際予備審査報 IPEA/4	吸告の送付通知(様式 1 6)を参照すること	
	出願番号 「/ J P 9 8 / 0 3 9 8 0	国際出願日 (日.月.年) 04	. 09. 98	優先日 (日.月.年) 0.5	5. 09. 97
	特許分類 (IPC) t. Cl ⁶ A61K31/52	// C07D473	/04, C07D47	73/20, C07D	473/22
出願人	(氏名又は名称) 協和醗酵工業株式会	生 ————————————————————————————————————			
1.	国際予備審査機関が作成したこの	 国際予備審査報告を 法	施行規則第57条(P	CT36条)の規定に	二従い送付する。
2.	この国際予備審査報告は、この表	紙を含めて全部で	5 ~-	ジからなる。	
	□ この国際予備審査報告には、 査機関に対してした訂正を含 (PCT規則70.16及びPCT この附属書類は、全部で	む明細書、請求の範囲	及び/又は図面も添 参照)		スはこの国際予備審
3.	この国際予備審査報告は、次の内	容を含む。			
	I x 国際予備審査報告の基礎	Ě			
	Ⅱ				
	Ⅲ x 新規性、進歩性又は産業	&上の利用可能性につ	いての国際予備審査幸	8告の不作成	
	Ⅳ □ 発明の単一性の欠如				
	V x PCT35条(2)に規定 の文献及び説明	する新規性、進歩性ス	スは産業上の利用可能	性についての見解、そ	それを裏付けるため
	VI 📗 ある種の引用文献				
	VII 国際出願の不備			•	
	VII 国際出願に対する意見				-
国際	予備審査の請求書を受理した日 31.03.99		国際予備審査報告を	作成した日 27.10.9	9
名称	及びあて先 日本国特許庁(IPEA/JP	·)	特許庁審査官(権限	のある職員)	4 P 9 2 8 2

中木 亜希

電話番号 03-3581-1101

3492

内線

郵便番号100-8915

東京都千代田区霞が関三丁目4番3号

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I.	<u> </u>	国際予備審査報	発告の基礎						
1.	1. この国際予備審査報告は下記の出願書類に基づいて作成された。 (法第6条 (PCT14条) の規定に基づく命令に 応答するために提出された差し替え用紙は、この報告書において「出願時」とし、本報告書には添付しない。 PCT規則70.16,70.17)								
	х	出願時の国際	出題書類						
		明細書	第 · ·	ページ、	出願時に提出されたもの				
	Ш	明細書	^免 第	^~~	国際予備審査の請求書と共に提出されたもの				
		明細書	第	<u> </u>	付の書簡と共に提出されたもの				
		74							
		請求の範囲		項、	出願時に提出されたもの				
		請求の範囲		項、	PCT19条の規定に基づき補正されたもの				
		請求の範囲 請求の範囲	· · · · · · · · · · · · · · · · · · ·	項、 項、	国際予備審査の請求書と共に提出されたもの 付の書簡と共に提出されたもの				
		請水の配置	я»						
		図面	第		出願時に提出されたもの				
	_	図面	第	ページ/図、	国際予備審査の請求書と共に提出されたもの				
		図面	第	ページ/図、	付の書簡と共に提出されたもの				
	\Box	m m a a a a a a	引まのかり 祭	ページ、	出願時に提出されたもの				
	Ш		刊表の部分 第 刊表の部分 第	ページ、	国際予備審査の請求書と共に提出されたもの				
ļ			列表の部分 第	~~	付の書簡と共に提出されたもの				
2.	-	上記の出願書類	質の言語は、下記に示 [・]	す場合を除くほか、こ(の国際出願の言語である。				
		! 割の事物は	て知の言語でもで		z				
	-	こ記の音類は、	下記の言語である		~				
	1	国際調査	のために提出されたF	PCT規則23.1(b)にい	う翻訳文の言語				
	Ì	=	則48.3(b)にいう国際		,				
					は55.3にいう翻訳文の言語				
			•						
3.		この国際出願に	は、ヌクレオチド又は	アミノ酸配列を含んで	おり、次の配列表に基づき国際予備審査報告を行った。				
				_ 1 ~ ***					
İ		_	出願に含まれる書面に						
				こフレキシブルディスク	1				
١					出された書面による配列表				
					出されたフレキシブルディスクによる配列表				
		□ 出願後に	:提出した書面による酢	尼列表が出願時における	国際出願の開示の範囲を超える事項を含まない旨の陳述				
		書の提出	があった	7701 - 1 2 1 - 2 2	・マカにトス和列末に釣得した和列が同一でなる岩の陣派				
			る配列表に記載したE があった。	記列とフレキシブルティ	マスクによる配列表に記録した配列が同一である旨の陳述				
1		音の挺山	111-87-71-0		·				
4		補正により、	下記の書類が削除され	た。	·				
		明細書	第						
		請求の範囲	第	項					
Ì	П	図面	図面の第	~-	ジ/図				
	_				and the second s				
5	. ∐	この国際予	備審査報告は、補充概]に示したように、補正	が出願時における開示の範囲を越えてされたものと認めら				
•		れるので、	その補止がされなかっ ける劇性の際に去食し	たものとして作成した なければならず、本報	。(PCT規則70.2(c) この補正を含む差し替え用紙は上 生に添けする。)				
		前1. にお	りる刊例の妖に考慮し	いみひねびみばひり、今報	. p.d 1 → 14m (J - 7 · 6 / 6 · 7 ·				
		•			•				
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ш.	新規性、進歩性又は産業上の利用可能性についての国際予備審査	E報告の不作成	1					
1. 次に関して、当該請求の範囲に記載されている発明の新規性、進歩性又は産業上の利用可能性につき、次の理由により 審査しない。								
	国際出願全体		Ì					
x	請求の範囲							
理由	:							
x	この国際出願又は請求の範囲 4	は、国際予備審査をすることを要しない						
	次の事項を内容としている(具体的に記載すること)。		i					
	請求の範囲4に記載された発明は、人の治 る。	療による処置方法の発明に該当す						
			Ì					
		•	1					
<u> </u>								
	明細書、請求の範囲若しくは図面(次に示す部分)又は請求の範		٠					
	記載が、不明確であるため、見解を示すことができない(具体的は	こ記載すること)。						
		•	l					
		•						
$ \Box$	全部の請求の範囲又は請求の範囲	が、明細書による十分な	ŗ					
	裏付けを欠くため、見解を示すことができない。							
		•						
×	請求の範囲4	_ について、国際調査報告が作成されていない。						
2.	ヌクレオチド又はアミノ酸の配列表が実施細則の附属書C (塩基 ガイドライン) に定める基準を満たしていないので、有効な国際	配列又はアミノ酸配列を含む明細書等の作成のための 予備審査をすることができない。)					
	■ 書面による配列表が提出されていない又は所定の基準を満た	していない。						
	□ フレキシブルディスクによる配列表が提出されていない又は	所定の基準を満たしていない。						

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v.	新規性.		川用可能性についての法第12条	(РСТЗ5条(2))	に定める見解、	それを裏付ける
1.	見解					
	新規性()	N)	請求の範囲 _ 請求の範囲 _	1-3	3, 5	有 無
	進歩性(I'S)	請求の範囲 _ 請求の範囲 _	. 1-3	3, 5	有 無
	産業上の	利用可能性(IA)	請求の範囲 _ : 請求の範囲 _	1 – :	3, 5	有

2. 文献及び説明 (PCT規則70.7)

- 1)請求の範囲1-3,5は、国際調査報告で引用された文献
 - 1. JP, 2613355, B2
 - 2. JP, 2613352, B2 3. JP, 6-239862, A

に記載されているので新規性及び進歩性を有しない。

文献1及び2には、本願の請求の範囲3に記載された化合物を有効成分とするパー キンソン氏病治療剤が記載されている。

文献3には、本願の請求の範囲3に記載された化合物は、パーキンソン氏病を再現 するモデルとして知られているハロペリドール誘発カタレプシーに対して、抑制作用 を示したことが記載されている。

ここで、文献1~3にも記載されているように、パーキンソン氏病は黒質ー線条体系ドパミン神経の変性・細胞死に基づく疾患であることから、パーキンソン氏病は神 経変性疾患の一つであると認められる。

してみると 文献1~3には、本願の請求の範囲3に記載された化合物を有効成分 とする神経変性疾患治療剤に係る発明、及び、神経変性疾患治療剤を製造するため の、本願の請求の範囲3に記載された化合物の使用に係る発明が記載されていると認 められる。

2) 請求の範囲1, 2, 5は、国際調査報告で引用された文献4. JP, 6-47539, B2 に記載されているので新規性及び進歩性を有しない。

文献4には、1,3,7ートリメチルー8ー[3-(4-ジメチルアミノカルボニルピペラジノ)プロピル]キサンチンを有効成分とするアルツハイマー病治療用医薬 品組成物が記載されており、1、3、7-トリメチル-8-[3-(4-ジメチルア ミノカルボニルピペラジノ)プロピル]キサンチンは、本願の請求の範囲2に記載の 化合物に包含される。

本願明細書第9頁第13~17行には、神経変性疾患としてアルツハイマー病が例 示されている。

してみると、 文献4には、本願の請求の範囲2に記載された化合物を有効成分とす る神経変性疾患治療剤に係る発明、及び、神経変性疾患治療剤を製造するための、本 願の請求の範囲2に記載された化合物の使用に係る発明が記載されていると認められ る。

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補充欄(いずれかの欄の大きさが足りない場合に使用すること)

第 V 欄の続き

3) 請求の範囲1, 2, 5は、国際調査報告で引用された文献5. US, 4772607, A により進歩性を有しない。

文献5には、1位と3位に低級アルケニルを有し、8位にシクロアルキルを有する化合物がアルツハイマー病の治療に用いることができることが示唆されている。そこで、薬理試験等を行うことにより、1位と3位に低級アルケニルを有し、8位にシクロアルキルを有する化合物がアルツハイマー病の治療に有効であることを確認することは、当業者であれば容易に成し得たことと認められる。そして、本願の請求の範囲1,2,5に係る発明において奏せられる効果についても、文献5の記載から当業者が予測できない程の格別顕著な効果が奏せられているとも認められない。

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